

# Mice Exposed to Combined Chronic Low-Dose Irradiation and Modeled Microgravity Develop Long-Term Neurological Sequelae

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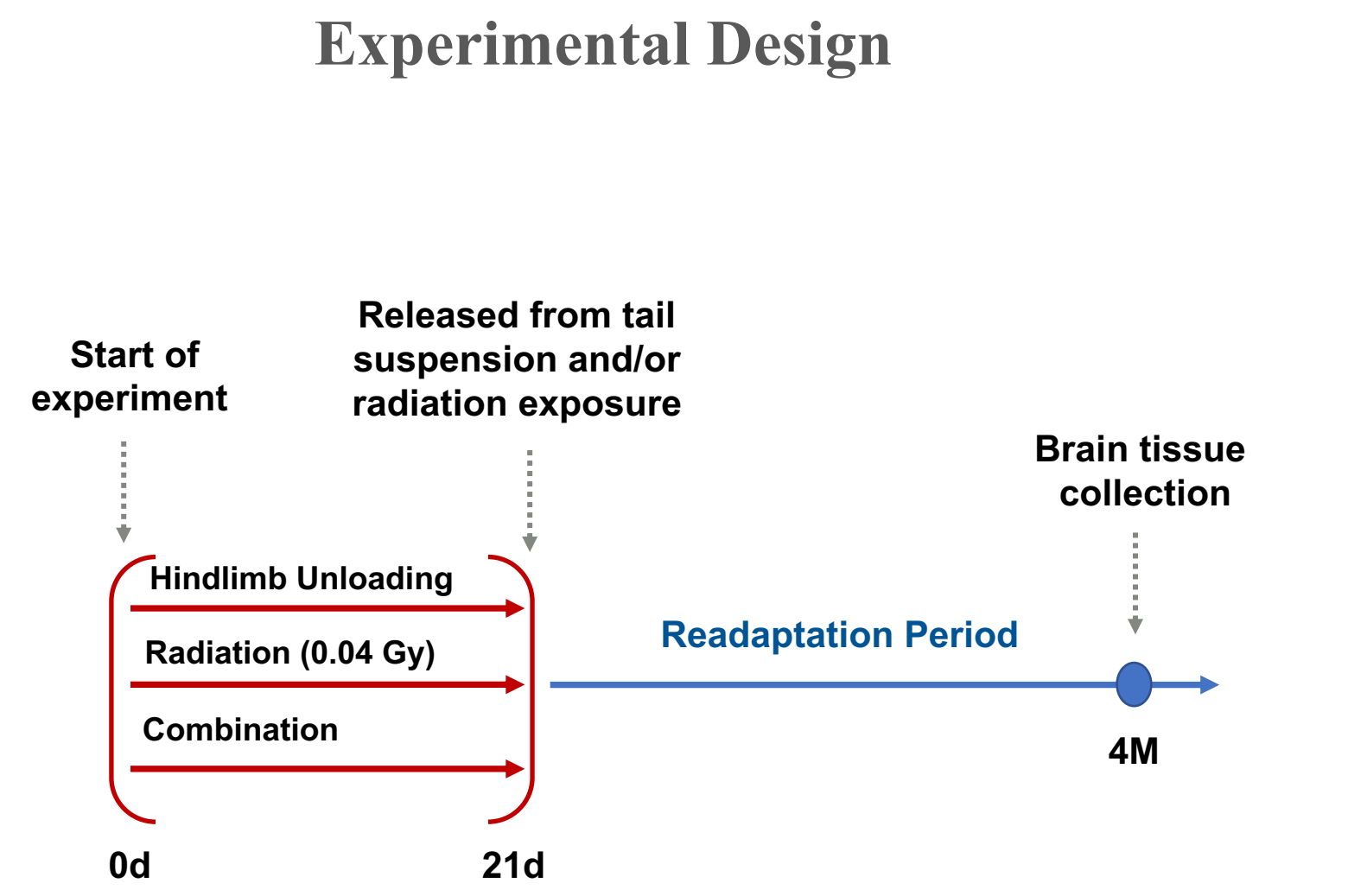
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## Introduction

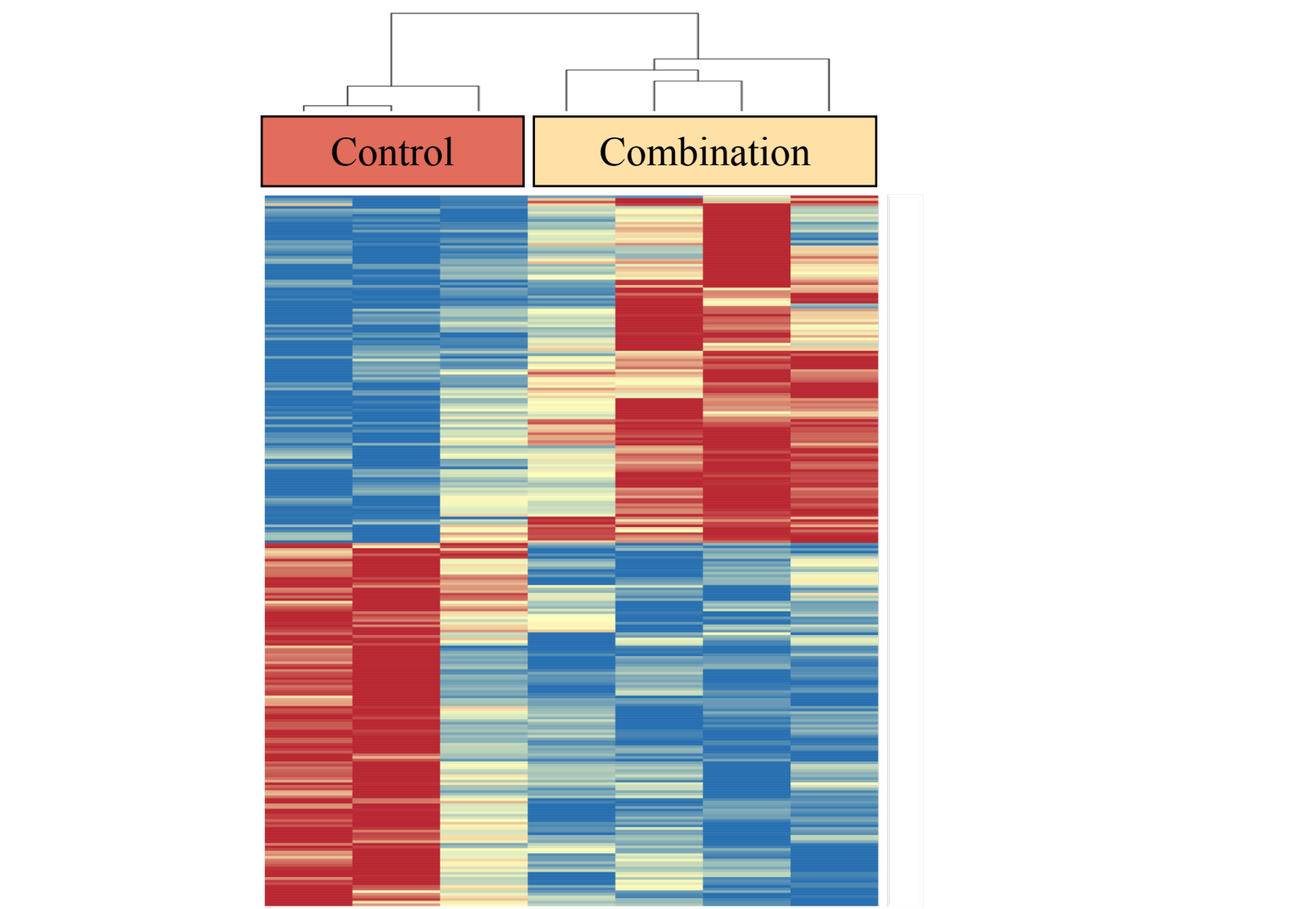
How rapidly do astronauts recover neurologically from spaceflight? Evidence suggests that astronauts can experience cognitive impairment while in space, but we don't know how long gene expression changes in brain tissue persist once returned to Earth. This study works towards the long-term goal of uncovering the length of time that astronauts need to in order to re-adapt to Earth after returning from their missions.

In our experiment, mice were exposed to modeled microgravity (hindlimb unloading) and low-dose radiation (cobalt plates). RNA sequencing data was collected from brain tissue and analyzed for differentially expressed genes and their corresponding functions.

## Results



### Differentially Expressed Genes Profile for Combination Group



## Discussion

- The combination group and each individual conditions **do not share** any overlapping differentially expressed genes. Each group had a **distinct set** of differentially expressed genes.
- Differentially expressed genes in the combination group suggest an **reduced transcriptional machinery, increased neurogenesis and neuropeptide production, dysregulated cell structure and cell signaling** at the 4 month timepoint.

## Methods

### Microgravity Model

Hindlimb unloading to create fluid-shift towards the head.

### Low-Dose Radiation

Cobalt plates that release low-dose radiation (0.04Gy) as gamma rays.

### RNA-sequencing

Measures gene expression from brain tissue.

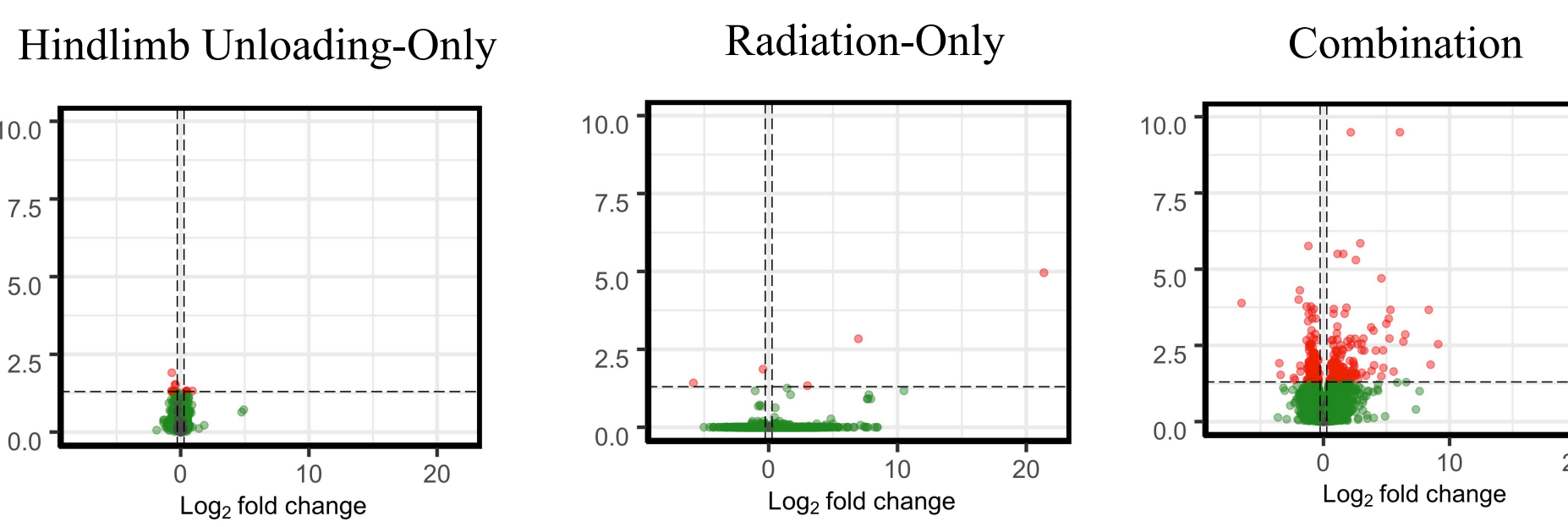
### GeneLab computational pipeline

Processes RNA-sequencing data into differentially expressed genes.

### Higher-Order Analyses

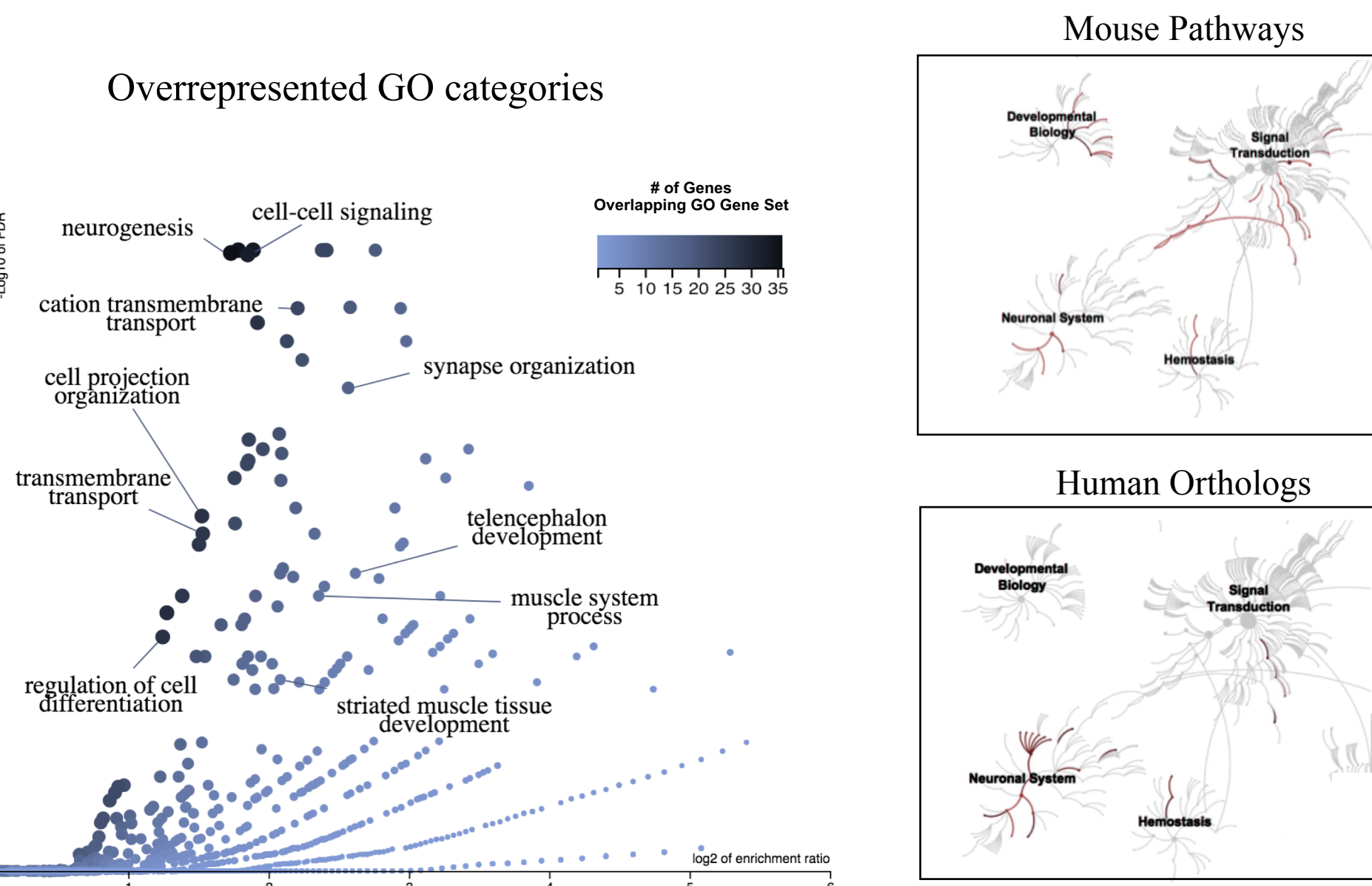
Computational tools WebGestalt for gene ontology analysis and Reactome for pathway analysis

### Differential Gene Expression Occurs Primarily with Combined Spaceflight Factors



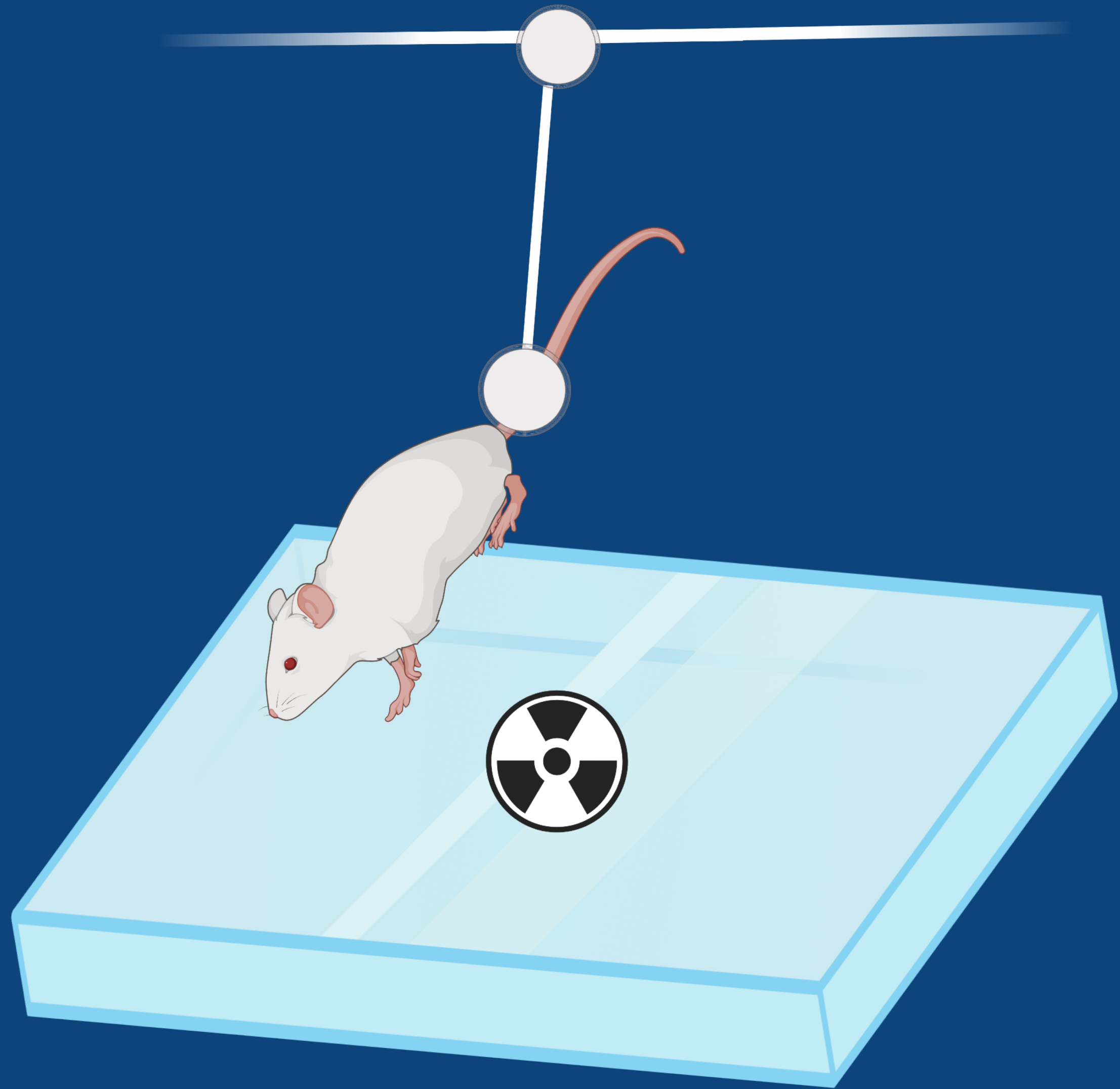
Each plotted point is a gene. Differentially expressed genes are in **red**, which means it has met the adjusted p-value and Log<sub>2</sub> fold-change threshold for significance ( $p \leq 0.05$ ,  $|\log_2 FC| > 0.263$ ). If it has only met the adjusted p-value threshold, it is in **green**.

### Gene Ontology (GO) and Pathway Analyses



A combination of spaceflight-relevant factors (fluid-shift and radiation) created a different gene expression profile than either factor individually.

Gene expression differences can persist for at least 4 months after a 21-day exposure to a combination of fluid-shift and radiation in the brain tissue of mice.



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